

48. A composition comprising the synthetic oligonucleotide of claim 41 and a pharmaceutically acceptable carrier.

49. (NEW) The synthetic oligonucleotide of claim 34, which is modified to include a peptide nucleic acid (PNA).

50. (NEW) The synthetic oligonucleotide of claim 41, which is modified to include a peptide nucleic acid (PNA).

REMARKS

I. Introduction

In response to the Office Action dated May 15, 2002, claims 31, 36-40, 42, 43 and 46 have been amended, claims 26-30, 32, 33 and 35 have been canceled, and new claims 49-50 have been added. Claims 31, 34 and 36-50 remain in the application. Entry of these amendments, and reconsideration of the application, as amended, is requested.

II. Information Disclosure Statement

Applicants respectfully request the Examiner consider and initial in the column indicated on Form 1449 that was included with the Information Disclosure Statement filed on May 6, 2002, to indicate consideration of the Szyf patent (No. 5,578,716) listed at the top of this form. While the copy of this Form 1449 provided with the Advisory Action dated August 30, 2002, includes the Examiner's initials in the appropriate column next to each of the other listed references, it appears that the Examiner's initials may have been inadvertently omitted from the box adjacent the Szyf patent.

III. Claim Amendments

Applicants' attorney has made amendments to the claims as indicated above. These amendments were made to clarify the language of the claims, and introduce no new matter. Claims 31, 36, 43 and 46 were amended merely to incorporate the language of the parent claim from which

they previously depended and/or to clarify the recited length limitations, and thus are of identical scope. The amendment to claims 31, 43 and 46 is supported by the specification at page 28, line 24, and page 35, line 4, as well as SEQ ID NO: 1, 2, 18-56, 58-73, 75-101, 103, 105, 107 and 109. Claims 37-39 were amended to clarify which of the recited nucleotide sequences fall within the length limitations already appearing in those claims. Claims 40 and 42 were amended to delete the reference to PNA, which subject matter is now addressed separately in new claims 49 and 50. Accordingly, the new and amended claims are supported by the application as originally filed, and entry of these amendments is respectfully requested.

IV. Examiner Interview

The amendments to the claims presented herein were discussed with Examiner Wilson during a telephone conference with Applicants' undersigned representative on August 14, 2002. Applicants gratefully acknowledge and appreciate the Examiner's helpful comments during this interview. These amendments are presented in a good faith belief to put the application in condition for allowance. Should the Examiner find that further action is required to put the application in condition for allowance, the courtesy of a telephone call to Applicants' representative to indicate the action required would be appreciated.

V. Non-Art Rejection

Claims 27-30, 35-40, and 42 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The cancellation of claims 27-30 and 35 renders the rejection of these claims moot. (For the record, however, Applicants continue to maintain that there is a distinction between the permissible recitation of a functional limitation, as in claims 27-30 and 35, and recitation of intended use.) The rejection of claims 36-40 and 42 is rendered moot by the amendments.

The rejection of claims 36-39 is based on the recitation of "approximately", which is regarded by the Examiner as confusing because these claims are allegedly drawn to sequences of a specific size. Although these claims have been amended to clarify the sizes, Applicants wish to

address this statement for the record. With respect to claim 36, Applicants respectfully disagree with the statement in the Office Action, as "approximately" modifies the "oligonucleotide", which "comprises a nucleotide sequence selected from the group consisting of" the recited sequences, and each of the recited sequences falls within the recited range. Claims 37-39 have been amended to recite only those nucleotide sequences that fall within the length recited for those claims. Accordingly, withdrawal of this rejection is respectfully requested.

Although claims 26, 31, 43 and 46 were not rejected under 35 U.S.C. §112, second paragraph, it appears from the Advisory Action that further review by the Examiner has resulted in a determination that claims reciting "at least approximately" are indefinite because it is unclear which portions of the sequence are to be excluded when the approximate size is significantly smaller than the full sequence as disclosed in the recited SEQ ID Nos. Accordingly, the arguments presented herein are applicable to the language preserved from previous claim 26 as well as claims 31, 43 and 46.

Applicants maintain that a sequence that is "significantly smaller" is not "approximately" the same size, and that such a distinction is clear on its face to any person of skill in the art due to the plain and ordinary meaning of the word "approximate". "Approximate" is defined in Webster's Collegiate Dictionary, 10th Edition as "nearly correct or exact" (copy of definition attached herewith). The "approximate" size therefore clearly excludes significantly smaller oligonucleotides.

The specification teaches (e.g., at page 16, lines 21-25) that the synthetic oligonucleotide can be approximately 5 to approximately 70 nucleotides in length, or preferably approximately 15 to approximately 50 nucleotides in length, or more preferably approximately 20 to approximately 30 nucleotides in length. Because some of these ranges differ by 5 nucleotides, it is apparent that "approximately" does not include differences in length of 5 or more nucleotides. Accordingly, it is clear to those skilled in the art that the recitation of "at least approximately 30 nucleotides" does not include an oligonucleotide of, for example, only 25 nucleotides in length or less. Those skilled in the art do recognize that one could prepare an oligonucleotide that is equivalent to the recited oligonucleotide of 30 nucleotides in length, as disclosed in Applicants' specification, by deleting just

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a few nucleotides, so long as the 5mCpG dinucleotide is retained. Consistent with this is the teaching in the specification at page 28, line 24, and page 35, line 4, as well as SEQ ID NO: 1, 2, 18-56, 58-73, 75-101, 103, 105, 107 and 109, all of which teach use of a synthetic oligonucleotide that is 26 nucleotides in length.

To facilitate prosecution, Applicants have omitted "approximately" from the amended claims presented herein. While Applicants acknowledge that significantly smaller oligonucleotides are clearly excluded from the claimed subject matter, only such significantly smaller oligonucleotides are intended to be excluded from Applicants' claims. Applicants do not relinquish subject matter that is equivalent to the literal scope of the claims, but differs from the literal structure by only trivial modifications, such as deletion of a few nucleotides.

Although claims 31, 43 and 46 have not been formally rejected by the Examiner, comment (1) in the Advisory Action dated August 30, 2002, suggests that the Examiner will not allow claims reciting "at least approximately 30 nucleotides". As discussed above, the teachings of the specification support "at least 26 nucleotides" as equivalent to "at least approximately 30 nucleotides". To facilitate prosecution, Applicants have amended claims 31, 43 and 46 to substitute this equivalent language.

VI. Prior Art Rejections

On page 3 of the Office Action, claims 26-30, 32, and 33 were rejected under 35 U.S.C. §103(a) as being unpatentable over Froehler et al., U.S. Patent No. 5,830,653. The rejection of these claims is rendered moot in view of the cancellation of claims 26-30, 32 and 33.

VII. Acknowledgement of Allowable Claims

On page 3 of the Office Action, claims 31, 43 and 46 were objected to as being based upon a rejected base claim, and claims 34, 41, 44, 45, 47 and 48 were indicated as being free of the prior art. Applicants have amended claims 41, 43 and 46 to incorporate, in independent form, all limitations of the base claim. Applicants appreciate the Examiner's acknowledgement of allowable subject matter.

VIII. Conclusion

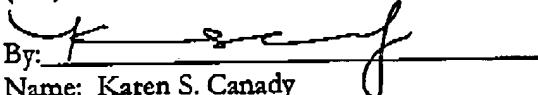
In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

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APPENDIX: CLAIMS IN MARKED-UP FORM

31. (AMENDED) [The synthetic oligonucleotide of claim 27,] A synthetic oligonucleotide of at least 26 nucleotides in length and comprising a 5mCpG dinucleotide, wherein the 5mC is a C-5 methylcytosine, and which comprises a nucleotide sequence selected from the group consisting of TGACGTCA and SEQ ID NOS: 1-4, 6-12, 14-15, 18-101, 103, 105, 107 and 109, wherein the synthetic oligonucleotide comprises a phosphorothioate nucleotide.

36. (AMENDED) The synthetic oligonucleotide of claim 34, wherein the oligonucleotide is [approximately] 15 to [approximately] 70 nucleotides in length.

37. (AMENDED) The synthetic oligonucleotide of claim 34, wherein the oligonucleotide is [approximately] 15 to [approximately] 50 nucleotides in length, and wherein the nucleotide sequence is selected from the group consisting of SEQ ID NOS: 1, 2, 4, 6-8, 13, 18-101, 103, 105, 107 and 109.

38. (AMENDED) The synthetic oligonucleotide of claim 34, wherein the oligonucleotide is [approximately] 20 to [approximately] 30 nucleotides in length, and wherein the nucleotide sequence is selected from the group consisting of SEQ ID NOS: 1, 2, 4, 6-8, 13, 18-101, 103, 105, 107 and 109.

39. (AMENDED) The synthetic oligonucleotide of claim 34, wherein the oligonucleotide is [approximately] 30 nucleotides in length, and wherein the nucleotide sequence is selected from the group consisting of SEQ ID NOS: 1, 2, 4, 6-8, 13, 18-101, 103, 105, 107 and 109.

40. (AMENDED) The synthetic oligonucleotide of claim 34, which comprises a phosphorothioate, [peptide nucleic acid (PNA),] deoxyribonucleic guanidine (DNG), or ribonucleic guanidine (RNG) oligonucleotide.

42. (AMENDED) The synthetic oligonucleotide of claim 41, which comprises a phosphorothioate, [peptide nucleic acid (PNA),] deoxyribonucleic guanidine (DNG), or ribonucleic guanidine (RNG) oligonucleotide.

43. (AMENDED) A pharmaceutically acceptable salt of [the synthetic oligonucleotide of claim 26] a synthetic oligonucleotide of at least 26 nucleotides in length and comprising a 5mCpG dinucleotide, wherein the 5mC is a C-5 methylcytosine, and wherein the synthetic oligonucleotide comprises a phosphorothioate nucleotide.

46. (AMENDED) A composition comprising [the synthetic oligonucleotide of claim 26] a synthetic oligonucleotide of at least 26 nucleotides in length and comprising a 5mCpG dinucleotide, wherein the 5mC is a C-5 methylcytosine, and wherein the synthetic oligonucleotide comprises a phosphorothioate nucleotide, and a pharmaceutically acceptable carrier.



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Springfield, Massachusetts, U.S.A.

syn APPROVE, ENDORSE, SANCTION, ACCREDIT, CERTIFY mean to have or express a favorable opinion of. APPROVE often implies no more than this but may suggest considerable esteem or admiration (the parents approve of the marriage). ENDORSE suggests an explicit statement of support (publicly endorsed her for Senator). SANCTION implies both approval and authorization (the President sanctioned covert operations). ACCREDIT and CERTIFY usu. imply official endorsement attesting to conformity to set standards (the board voted to accredit the college) (must be certified to teach).

approved school *n* (1932) *Brit*: a school for juvenile delinquents

ap-prox-i-mate *v*, *past* *ap-prox-i-mat-ed* *adv* [L. *approximans*, pp. of *approximare*] to come near, fr. L. *ad* + *proximare* to come near — more at PROXIMATE] (15c) 1: located close together (as leaves) 2: nearly correct or exact (as a solution) — *ap-prox-i-mately* *adv*

ap-prox-i-mate *v*, *past* *ap-prox-i-mat-ed* *adv* (15c) 1: a: to bring near or close b: to bring (cut edges of tissue) together 2: to come near to or be close to in position, value, or characteristics (a child tries to ~ his parents' speech) — *ap-prox-i-mately* *adv*

ap-prox-i-mation *v*, *past* *ap-prox-i-mat-ed* *adv* (15c) 1: the act or process of drawing together 2: the quality or state of being close or near (as ~ to the truth) (as ~ of justice) 3: something that is approximate; esp: a mathematical quantity that is close in value to but not the same as a desired quantity — *ap-prox-i-mative* *ap-prox-i-mat-iv* *adj*

ap-pear-tenance *v*, *past* *ap-pear-ten-ant-ed* *adv* (14c) 1: an incidental right (as a right-of-way) attached to a principal property, right and passing in possession with it 2: a subordinate part or adjunct (the ~ of welcome is function and ceremony —Shak.) 3 *pl*: accessory objects: APPARATUS

ap-pur-tin-ent *v*, *past* *ap-pur-tin-ent-ed* *adv* [ME *appertenent*, fr. MF, fr. OF, pp. of *appartenir* to belong — more at APPERTAIN] (15c) 1: constituting a legal accomplishment 2: AUXILIARY, ACCESSORY — *appurtenance* *n*

ap-prax-ia *v*, *past* *ap-prax-ia-ed* *adv* [NL, fr. Gk. *apraction*, fr. *a-* + *praxis* action, fr. *prōs* to do — more at PRACTICAL] (ca. 1881): loss or impairment of the ability to execute complex coordinated movements without impairment of the muscles or senses — *apractic* *v*, *practic* *ap-prax-ic* *adj*

ap-rés *v*, *past* *ap-rés-ed* *adv* [F *après*, fr. *après* after] (1967): AFTER (as *tear*) — usu. used in combination (*après-theater party*)

ap-rés-aid *v*, *past* *ap-rés-aid-ed* *adv* [F *après* after + *aid* ski, skiing] (1952) 1: social activity (as at a ski lodge) after a day's skiing

ap-spi-cit *v*, *past* *ap-spi-cit-ed* *adv* [after, or earlier, abracoon, ultim. *in Ar* *al-**spicere* the apricot, ultim. fr. L. *(per)succum* *praeceps*, lit., early ripening (peach) — more at PRECOCIOUS] (1551) 1: a: the oval orange-colored fruit of a temperate-zone tree (*Prunus armeniaca*) resembling the related peach and plum in flavor b: a tree that bears apricots 2: a variable color averaging a moderate orange

April *v*, *past* *ap-ril* *adv* [ME, fr. OF & L. *OF* *avril*, fr. L. *Aprilis*] (bef. 12c) 1: the 4th month of the Gregorian calendar

April fool *n* (1687): the butt of a joke or trick played on April Fool's Day; also: such a joke or trick

April Fools' Day *n* (1903): April 1 characteristically marked by the playing of practical jokes

ap-ri-od *v*, *past* *ap-ri-od-ed* *adv* [L. *apri-* + *od-* *or*, *or*] *adj* [L. *lit.*, from the former] (1652) 1: a: DEDUCTIVE b: relating to or derived by reasoning from self-evident propositions — compare A POSTERIORI c: presupposed by experience 2: a: being without examination or analysis: *presumptive* b: formed or conceived beforehand — a *pri-* *ori* *adv* — *ap-ri-od-ity* *v*, *ap-ri-od-ed* *adv*

apron *v*, *past* *apron-ed* *adv* [after *attrib* [ME, alter. (resulting fr. false division of *an apron*), fr. MF *napron*, fr. L. *nappon*, dim. of *nappa* cloth, modif. of L. *mappa* napkin] (15c) 1: a: garment usu. of cloth, plastic, or leather usu. tied around the waist and used to protect clothing or adorn a costume 2: something that suggests or resembles an apron in shape, position, or use: a: the lower member under the sill of the interior casing of a window b: an upward or downward vertical extension of a bathroom fixture (as a sink or tub) c: an endless belt for carrying material d: an extensive fan-shaped deposit of detritus e: the part of the stage in front of the proscenium arch f: the arca along the waterfront edge of a pier or wharf g: a shield (as of concrete or gravel) to protect against erosion (as of a waterway) by water h: the extensive paved part of an airport immediately adjacent to the terminal area or hangars — *aproned* *v*, *apron-ed* *adv*

apron string *n* (1542): the string of an apron — usu. used in pl. as a symbol of dominance or complete control (though 40 years old he was still tied to his mother's apron strings)

ap-rop-o-sis *v*, *past* *ap-rop-o-sis-ed* *adv* [F *à propos*, lit., to the purpose] (1668) 1: at an opportune time: SEASONABLY 2: BY THE WAY

ap-rop-o-sis *adj* (1686): being both relevant and opportune **syn** RELEVANT

ap-rop-o-sis *prop* (1910): APPROPPOS OF

ap-rop-o-sis *prop* (1746): with regard to: CONCERNING

ap-rot-ic *v*, *past* *ap-rot-ic-ed* *adv* [Fr. *- + proton* + *-ic*] (1931) of a solvent: incapable of acting as a proton donor

apse *v*, *past* *apse* *adv* [ML & L: ML *apsa*, fr. L.] (1822) 1: *APSI* 1 2: a projecting part of a building (as a church) that is usu. semicircular in plan and vaulted

ap-se-dal *v*, *past* *ap-se-dal-ed* *adv* (1846): of or relating to an apse or apsis

ap-sis *v*, *past* *ap-sis-ed* *adv* [NL *apsis*, *apsis*, fr. L. *arch*, orbit, fr. Gk. *apsis*, *apsis*, fr. *apttein* to fasten] (1658) 1: the point in an astronomical orbit at which the distance of the body from the center of attraction is either greatest or least 2: *APSE* 2

apt *v*, *past* *apt-ed* *adv* [ME, fr. L *aptus*, lit., fastened, fr. pp. of *apere* to fasten; akin to L *apere* to grasp, obtain, *apud* near, *Hitt* *hap-* to attach] (14c) 1: unusually fitted or qualified: *READY* (proved an ~ tool in the hands of the conspirators) 2: a: having a tendency: *LIKELY* (plants ~ to suffer from drought) b: ordinarily disposed: *INCLINED* (~ to accept what is plausible as true) 3: suited to a purpose; esp: being to the point (as ~ quotation) 4: keenly intelligent and responsive